"A STUDY ON THE PREVALENCE OF PERIPHERAL VASCULAR DISEASE IN CHRONIC RENAL FAILURE"

Dissertation submitted in partial fulfillment of the

Requirement for the award of the Degree

of

DOCTOR OF MEDICINE

BRANCH I –GENERAL MEDICINE

MARCH 2009

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

MADURAI MEDICAL COLLEGE, MADURAI

CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY OF PREVALENCE OF PERIPHERAL VASCULAR DISEASE IN CHRONIC RENAL FAILURE"** submitted by **Dr.S.JAYACHANDRAN** to The Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment for the award of Doctor of Medicine is a bonafide work carried out by him under my guidance and supervision during the academic year 2007-2008. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

DR.A.AYYAPPAN, M.D.,
PROFESSOR AND H.O.D.,
DEPARTMENT OF MEDICINE,
MADURAI MEDICAL COLLEGE,
MADURAI.

DECLARATION

I**, Dr.S.JAYACHANDRAN**, solemnly declare that the dissertation titled **"A STUDY ON PREVALENCE OF PERIPHERAL VASCULAR DISEASE IN CHRONIC RENAL FAILURE"** has been prepared by me. This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of MD Degree Branch I (General Medicine) It was not submitted to the award of any degree/diploma to any University either in part or in full previously.

Place: Madurai

Date: **Dr.S.JAYACHANDRAN**

ACKNOWLEDGEMENT

At the outset I wish to thank our **Dean Dr.SIVAKUMAR, M.S.,** for permitting me to carry out this study in our hospital.

I sincerely thank my beloved **Professor and H.O.D. of Medicine Dr.A.AYYAPPAN M.D.,** for his encouragement and valuable guidance to the study.

I express my sincere thanks to our Professor **DR.P.THIRUMALAI KOZHULUNDU SUBRAMANIAM, M.D., DIRECTOR, INSTITUTE OF MEDICINE, MADRAS MEDICAL COLLEGE** for his moral support and encouragement to the study

I am grateful to our Prof**.Dr.V.RAJAGOPAL, H.O.D. Vascular Surgery** and **Asst.Prof. Department of Vascular Surgery** for their guidance from the beginning and throughout the course of the study.

I sincerely thank **Prof.DR.SHANMUGAPERUMAL**, H.O.D.OF NEPHROLOGY for his valuable guidance in taking up this study and in defining the criteria for the study.

I am profoundly grateful to our Professors; **Dr.P.SELVARAJ,**

Dr.M.KAMARAJ, Dr.MOSES K. DANIEL, Dr.V.VADIVEL MURUGAN,

Dr.D.D..VENKATARAMAN and Dr.M.MUTHAIAH for their inspiration and suggestions during the course of the study.

I am thankful to our Assistant Professors; **Dr.S.SOMASUNDARAM, DR.M.JERALD MAJELLAH, DR.J.SANGUMANI and Dr.BALAJINATHAN and DR.SHEELA** for their valuable suggestions.

I am thankful to our **C.R.R.I. Dr.KIRTHIKA** for her immense co-operation in mobilizing patients to the Department of Vascular Surgery and in measuring the Ankle brachial index.

I also thank the technician at the Department of Vascular Surgery, Madurai Medical College for their profound help in measuring the ankle brachial index at the department.

I wish to acknowledge all those who have directly or indirectly helped me to complete this work in great success.

Last but not the least; I sincerely thank all the patients who participated in the study for their co-operation.

ABBREVIATIONS

CKD	: CHRONIC KIDNEY DISEASE
ESRD	: END STAGE RENAL DISEASE
PAD	: PERIPHERAL VASCULAR DISEASE
ABI	: ANKLE BRACHIAL INDEX
CRF	: CHRONIC RENAL FAILURE
GFR	: GLOMERULAR FILTRATION RATE
PAOD	: PERIPHERAL ARTERIAL OBSTRUCTIVE DISEASE
CRP	: C REACTIVE PROTEIN
HsCRP	: HIGH SENSITIVE C REACTIVE PROTEIN
IL	: INTERLEUKIN
ADP	: ADENOSINE DI PHOSPHATE
cAMP	: CYCLIC ADENOSINE MONOPHOSPHATE
DNA	: DEOXY RIBONUCLEIC ACID
SBP	: SYSTOLIC BLOOD PRESSURE
DBP	: DIASTOLIC BLOOD PRESSURE
USRDS	: UNITED STATES RENAL DATA SYSTEM
CLI	: CRITICAL LEG ISCHAEMIA
CHD	: CORONARY HEART DISEASE
ECG	: ELECTROCARDIOGRAM
CLI	: CRITICAL LEG ISCHAEMIA

CONTENTS

1. INTRODUCTION

The world is facing a global epidemic of chronic kidney disease. As the morbidity and mortality from infectious diseases decline, life expectancy increases and chronic degenerative diseases have become more prevalent. CKD is unique amongst the chronic-non infectious illnesses in that there is a very real window of opportunity to continue living comfortably in spite of being terminally ill[1].

It has been estimated from population survey data that at least 6% of the adult population in the United States has chronic kidney disease at stages 1 and 2. An unknown subset of this group will progress to more advanced stages of CKD. An additional 4.5% of the U.S. population is estimated to have stages 3 and 4 CKD.The most frequent cause of CKD is diabetic nephropathy, most often secondary to Type 2 Diabetes mellitus[2]. India, being the Diabetic capital of the world and diabetic nephropathy being the commonest cause of CKD, the prevalence of PVD is on the rise. There are about 7.85 million CKD patients in India[3].

Cardiovascular disease is the leading cause of morbidity and mortality in patients at every stage of CKD. The incremental risk of cardiovascular disease in those with CKD compared to the age and sex matched general population ranges from 10-20 folds, depending on the stage of CKD[2].

The increased incidence of Peripheral vascular disease in CKD is due to the higher susceptibility to atherosclerosis. While due attention is provided to the detection of coronary artery disease in CKD patients, PAD, that is associated with a high mortality rate is not usually assessed in these patients. This is not only due to the

lack of awareness of the remarkably high prevalence of PAD among CKD patients but to the asymptomatic nature of the disease, fewer than 50% of patients with PAD are symptomatic, thus defining a population with subclinical PAD[2].

The alarming increase in the number of patients with clinical and subclinical peripheral vascular disease in chronic renal failure calls for the need of screening all patients with CRF for PVD. A risk free, cost effective, non-invasive approach to screen all patients with CKD for PAD is necessary. The resting ABI (Ankle Brachial Index) is a sensitive and specific screening test used for establishing the diagnosis of PAD[4].

Individuals with asymptomatic PAD should be identified in order to offer therapeutic interventions known to diminish their increased risk of myocardial infarction, stroke, and death. This study is designed to determine the prevalence of PAD affecting the lower limbs in a population of CRF patients using the Ankle Brachial index.

REVIEW OF LITERATURE

PERIPHERAL ARTERIAL DISEASE

DEFINITION

PAD is defined as a clinical disorder in which there is a stenosis or occlusion in the aorta or arteries of the limbs[2].

Atherosclerosis is the leading cause of PAD in patients >40 years old. Other causes include thrombosis, embolism, vasculitis, fibromuscular dysplasia, entrapment, cystic adventitial disease, and trauma. The highest prevalence of atherosclerotic PAD occurs in the sixth and seventh decades of life. As in patients with atherosclerosis of the coronary and cerebral vasculature, there is an increased risk of developing PAD in cigarette smokers and in patients with diabetes mellitus, hypercholesterolemia, hypertension or hyperhomocysteinemia[2].

PATHOLOGY

Segmental lesions causing stenosis or occlusion are usually localized to large and medium sized vessels. The pathology of the lesions includes atherosclerotic plaques with calcium deposition, thinning of the media, patchy destruction of muscle and elastic fibres, fragmentation of the internal elastic lamina and thrombi composed of platelets and fibrin.

The primary sites of involvement are the abdominal aorta and the iliac arteries (30% of symptomatic patients), the femoral and the popliteal arteries (80-90% of the patients), and the more distal vessels, including the tibial and peroneal arteries (40-50% of patients).

Atherosclerotic lesions occur preferentially at arterial branch points, sites of increased turbulence, altered shear stress and intimal injury. Involvement of the distal vasculature is most common in elderly individuals and patients with diabetes mellitus.

PAD IN CHRONIC RENAL FAILURE

EPIDEMEOLOGY

PAD affects approximately 5% of adults in the United States who are 40 yrs and older[5]. The incidence of PAD increases with age. Data from the National Health and Nutrition Examination Survey (NHANES) reveals that the prevalence of PAD[6] in the age group 50 to 59 yr is 2.5% and increases to 14.5% in the age group of 70 yr[7]. Patients with impaired renal function have a greater than two-fold risk for developing PAD[8]. The **NHANES 1999–2000** found 24% of adults who were older than 40 yr and had a creatinine clearance < 60ml/min per 1.73 m2 to have an ABI < 0.9[8]. In the dialysis population, according to United States Renal Data System report, the incidence of clinical PAD is 15%.

INCIDENCE OF PAD IN INDIA

The overall prevalence of PVD among Indians is considerably low as compared to the Western patients. **Mohan et al** have reported the prevalence of PVD in South Indian diabetics to be 3.9%[8]; in Western series the prevalence ranges between 22 – 45%[9.] The prevalence of PVD in diabetics increases with age,

increasing from 3.2% in those below 50 yrs. of age to 33% in those above 80 yrs. of age[10]. The prevalence of PVD in diabetics also increases with the duration of diabetes from 15% to 45% at 10 to 20 years respectively after the diagnosis of diabetes[11]. In India, the number of diabetic patients above the age of 80 years or those with duration of diabetes more than 30 years is extremely low, thus explaining the low prevalence of PVD in diabetics

PAD IN ESRD

Among patients with end-stage renal disease (ESRD), peripheral arterial disease (PAD) is common and is associated with substantial morbidity and mortality. However, compared to other atherosclerotic diseases such as coronary and cerebrovascular disease, little is known concerning the epidemiology of lower extremity PAD in this population and limited information is available to guide treatment and preventive strategies.

Among patients with ESRD, estimates of the prevalence of PAD vary in part according to the specific population studied:

- In the United States, the overall prevalence of PAD among patients initiating dialysis is approximately 14 to 15 percent[12].
- Based on the **HEMO study** and **the USRDS database**, the prevalence of PAD is approximately 25 percent among chronic hemodialysis patients[13].
- Estimates were similar among prevalent dialysis patients included in the International Dialysis Outcomes and Practice Patterns Study **(DOPPS**) database, at 25 percent, but with significant variation noted geographically, ranging from 12 percent in Japan to 38 percent in Belgium[14].

- The prevalence of PAD appears to be particularly high in elderly dialysis populations. As an example, the North Thames Dialysis study of patients over the age of 70 reported PAD prevalence of 28 and 46 percent among chronic dialysis patients and incident patients, respectively[15].

The diagnosis of PAD in many of the aforementioned studies was made by chart review or patient questionnaire rather than by diagnostic testing. Therefore, these data probably underestimate the true prevalence of PAD in ESRD patients.

Prevalence of PVD[16]

Author and Year	Country	Prevalence Rate%	Reference Number
Migdalis et (1992)	Greece	44,0	4
Marinelli et al (1979)	U.S.A.	33.0	5
Walters et al (1192)	U.K.	23.5	6
Bhuripanyo et al (1992)	Thailand	21.3	7
Janka et al (1980)	Germany	16.0	8
De Silva et al (1993)	Sri Lanka	5.6	9
Mohan et al (1995)	South India	3.9	3

Prevalence of IHD in Relation to Duration of Diabetes

Author and Year	PVD Prevalence			
	At Diagnosis of Diabetes	After 10 years' Duration of Diabetes	After>20 years' Duration of Diabetes	Reference Number
Palumbo et al (1985)	8%	15%	42%	(10)
Mohan et al (1995)	2%	4%	8%	(3)

CLINICAL EVALUATION

Fewer than 50% of patients with PAD are symptomatic, although many have a slow or impaired gait. The most common symptom is intermittent claudication, which is defined as a pain, ache, cramp, numbness, or a sense of fatigue in the muscles; it occurs during exercise and is relieved by rest. The site of claudication is distal to the location of the occlusive lesion[2].

The Edinburgh Claudication Questionnaire has been shown to be 91 percent specific and 99 percent sensitive for diagnosing intermittent claudication in symptomatic patients. It is composed of a series of six questions and a pain diagram that are self-administered by the patient

Individuals with PAD Present in Clinical Practice with Distinct Syndromes17

Asymptomatic: Without obvious symptomatic complaint (but usually with a functional impairment).

Edinburgh Claudication Questionnaire

Question	*Response*	*Sensitivity (%)*	*Specificity (%)*
Do you get pain or discomfort in your leg(s) when you walk?	Yes (If patient answers no, then stop here)	99.3	13.1
Does this pain ever begin when you are standing still or sitting?	No	99.3	80.3
Do you get pain if you walk uphill or hurry?	Yes	98.8	13.1
Do you get pain if you walk at an ordinary pace on level ground?	Yes or no, dependent on severity of claudication	—	—
What happens if you stand still?	Pain gone in 10 minutes or less	90.6	63.9
Where do you get this pain?	Calf,* thigh, or buttock† marked	—	—

NOTE: *A positive classification for peripheral vascular disease requires the indicated responses for all questions.*

**—Definite claudicant = pain in calf.*

†—*Atypical claudication = pain in thigh or buttock (in the absence of calf pain).*

Adapted with permission from Leng GC, Fowkes FG. The Edinburgh Claudication Questionnaire: an improved version of the WHO/Rose Questionnaire for use in epidemiological surveys. J Clin Epidemiol 1992;45:1104.

***Classic Claudication*:** Lower extremity symptoms confined to the muscles with a consistent (reproducible) onset with exercise and relief with rest.

***"Atypical" leg pain*:** Lower extremity discomfort that is exertional, but that does not consistently resolve with rest, consistently limit exercise at a reproducible distance or meet all "Rose questionnaire" criteria

Critical Limb Ischemia: Ischemic rest pain, non-healing wound, or gangrene

Acute limb ischemia: The five "P's, defined by the clinical symptoms and signs that suggest potential limb jeopardy:

- Pain
- Pulselessness
- Pallor

- Paresthesias
- Paralysis (& polar, as a sixth “p”).

Frequently, these symptoms occur at night when the legs are horizontal and improve when the legs are in a dependent position. With severe ischemia, rest pain may be persistent.

Important physical findings of PAD include decreased or absent pulses distal to the obstruction, the presence of bruits over the narrowed artery, and muscle atrophy. With more severe disease, hair loss, thickened nails, smooth and shiny skin, reduced skin temperature, and pallor or cyanosis are frequent physical signs. In patients with critical limb ischemia, ulcers or gangrene may occur. Elevation of the legs and repeated flexing of the calf muscles produce pallor of the soles of the feet, whereas rubor, secondary to reactive hyperemia, may develop when the legs are dependent.

The time required for rubor to develop or for the veins in the foot to fill when the patient’s legs are transferred from an elvated to a dependent position is related to the severity of the ischemia and the presence of collateral vessels. Patients with severe ischemia may develop peripheral edema because they keep their legs in a dependent position much of the time. Ischemic neuropathy can result in numbness and hyporeflexia.

TABLE 3

Physical Findings for PVD with Sensitivity, Specificity, and Likelihood Ratios

Finding	*Description*	*ABI*	*Sensitivity (%)*	*Specificity (%)*	*LR+*
Abnormal pedal pulse	DP and PT pulses absent	< 0.9	63	99	44.6
	PT and DP pulses absent or one absent and one weak	< 0.9	73	92	9.0
Femoral artery bruit	Bruit present	< 0.8	20	96	4.7
	Bruit present	< 0.9	29	95	5.7
Cool skin	Unilateral cooler skin	< 0.9	10	98	5.8
Abnormal color	Pale, red, or blue	< 0.9	35	87	2.8

PVD = peripheral vascular disease; ABI = ankle-brachial index; LR+ = positive likelihood ratio; DP = dorsalis pedis; PT = posterior tibial.

Adapted with permission from McGee SR, Boyko EJ. Physical examination and chronic lower-extremity ischemia: a critical review. Arch Intern Med 1998;158:1360.

Although atherosclerosis in patients with diabetes is similar to that seen in non-diabetic patients[18], it is generalised, occurs prematurely and progresses at an accelerated pace.

Peripheral vascular disease in diabetics differs from that in non-diabetics in many aspects. In non diabetics the sites of occlusion are usually the infra-renal aorta, iliac and superficial femoral arteries, with sparing of distal vessels. Whereas, in diabetics, occlusive lesions occur in crural arteries, namely tibials and peroneals, with sparing of the arteries of the foot[19]. This characteristic vascular involvement in diabetics had made it possible to carry out vascular reconstruction, where proximal

vessels like popliteal is anastomosed to foot vessels like dorsalis pedis thus bypassing the obstructed tibial and peroneal vessels.

Clinical Differences in Diabetic and Non-Diabetic PVD

	Diabetic	Non Diabetic
Clinical	More common Younger age More rapid	Less common Older age Less rapid
Male/Female	M > F	M >> F
Occlusion	Multisegmental	Single segment
Vessels adjacent to occlusion	Involved	Not involved
Collateral vessels	Involved	Usually normal
Lower extremities	Both	Unilateral
Vessels involved	Proximal & distal	Proximal

PATHOGENESIS OF PERIPHERAL VASCULAR DISEASE IN CRF

Established risk factors for PAOD in the general population include increased age, hypertension, hyperlipidemia, smoking, diabetes mellitus, and coronary artery disease. Several unconventional cardiac risk factors, such as lipoprotein (a) levels, homocysteine levels, and chronic inflammation, are also associated with PAOD. There have been very few attempts to identify PAOD risk factors among patients with ESRD.

The HEMO Study found that diabetes mellitus and smoking were associated with PAOD among haemodialysis patients[21]. Age was significantly associated with PAOD among nondiabetic patients but not among diabetic patients. Black race was negatively associated with PAOD. Other conventional cardiac risk factors, such as male gender, hypercholesterolemia, and hypertension, were not associated with PAOD in the HEMO study.

Although conventional cardiac risk factors contribute to cardiovascular morbidity and death among patients with ESRD, they cannot fully account for the excess burden of cardiovascular disease in this group[21]. Preliminary evidence suggests that, as for other forms of cardiovascular disease, unconventional cardiac risk factors such as hyperparathyroidism, chronic inflammation, hyperhomocysteinemia, and apolipoprotein(a) levels may play significant roles in the development or progression of PAOD among patients with ESRD.

Vascular calcification seems to be extremely common among dialysis patients[22] and perhaps contributes to the development of PAOD. **Savage *et al.*[23]** (2observed that 75% of 24 patients with ESRD but without clinical evidence of cardiovascular disease had carotid or femoral artery calcified plaques. There is growing evidence that this phenomenon is associated with elevated serum phosphorous levels, elevated calcium and phosphorous product values, and hyperparathyroidism.

Among patients with ESRD, abdominal aortic calcification seems to be correlated with increased calcium and phosphorous product levels[24], and hyperphosphatemia and hyperparathyroidism have been demonstrated to be correlated with coronary, carotid, and femoral artery atherosclerosis among dialysis patients[25]. Goldsmith *et al.*[26] used skeletal surveys to document vascular calcification among 38

long-term hemodialysis patients. Those authors observed that calcification became more prevalent and more severe with time and that the rate of progression was determined by age, systolic BP, parathyroid hormone levels, and serum phosphorous and vitamin D levels.

Guerin *et al.*[27] recently demonstrated that the extent of vascular calcification in patients with ESRD is associated with the degree of arterial stiffness (as assessed in aortic pulse wave velocity measurements), serum fibrinogen levels, and the use of calcium-based binders. Arterial stiffening is correlated with the extent of atherosclerosis and has been demonstrated to be a powerful predictor of all-cause and cardiovascular mortality rates among hemodialysis patients[28]. These authors suggest that there may be a correlation between atherosclerotic disease burden and the degree of vascular calcification. However, the precise relationship between vascular calcification and peripheral vascular disease has yet to be fully elucidated.

There is growing evidence that chronic inflammation plays a role in the pathogenesis of atherosclerosis. Data from several prospective studies has demonstrated that elevated levels of the acute-phase reactant C-reactive protein (CRP) predicts an increased incidence of future cardiovascular events among a wide range of clinical populations, including individuals with no history of cardiovascular disease, those with angina, and those with a history of prior myocardial infarction[29].

Ridker *et al.*[30] directly evaluated the relationship between CRP levels and PAOD. Those authors identified 144 healthy men, participating in the Physicians' Health Study, who subsequently developed symptomatic PAOD, and it noted that baseline CRP levels were significantly higher for that group than for a group of control subjects who did not develop PAOD. CRP levels seem to be predictive of

cardiovascular mortality rates in the ESRD population, as they are in the general population [31].

An association between carotid artery atherosclerosis and CRP levels among patients with chronic renal insufficiency has also been demonstrated [32] However there are not any studies documenting a connection between lower-limb atherosclerosis and inflammation among patients with ESRD.

Lipoprotein(a) is a genetically determined risk factor for PAOD in the general population, and dialysis patients have significantly higher levels of lipoprotein(a) and low-molecular weight apolipoprotein(a) isoforms than do individuals with normal renal function. Low-molecular weight apolipoprotein(a) isoforms are associated with the presence of carotid artery plaques among hemodialysis patients. However, one study of patients undergoing peritoneal dialysis noted that lipoprotein(a) levels were not correlated with the presence of peripheral vascular disease [33]. Further research is needed to determine whether lipoprotein(a) confers a higher risk for the development or progression of PAOD in the ESRD population.

Hyperhomocysteinemia is a risk factor for lower-extremity PAOD and for the progression of PAOD in the general population [34]. There is an extraordinarily high prevalence of hyperhomocysteinemia among patients with ESRD [35], and it has been hypothesized that hyperhomocysteinemia may contribute to atherosclerosis in this population. Several studies have found that dialysis patients with the highest homocysteine levels exhibit a higher prevalence of PAOD, compared with patients with the lowest homocysteine levels[36].

Population studies have demonstrated that markers like soluble intercellular adhesion molecules - 1 (sICAM-1) and D-Dimer correlate significantly with the

development of PAD, while as markers like hsCRP and D-Dimer have a strong association with poorer lower extremity functioning in PAD patients. Factors recently reported to be associated with development of PAD are use of oral contraceptive agents and depression.

A strong relationship has been noted with IL-6 gene polymorphism in patients with PAD suggesting that inflammation may be involved in pathogenesis. However no relationship was noted with ACE polymorphism or V34Lpolymorphism.

NONINVASIVE TESTING

The history and physical examination are often sufficient to establish the diagnosis of PAD. An objective assessment of the paresence and severity of disease is obtained by noninvasive techniques. The non-invasive tests include

1. Resting Ankle-Brachial index
2. Exercise ABI
3. Segmental pressure examination
4. Pulse volume recordings

The Ankle-Brachial Index

$$\textbf{ABI} = \frac{\textbf{Lower extremity systolic pressure(mmHg)}}{\textbf{Higher brachial systolic pressure(mmHg)}}$$

The most efficient, objective and practical means of documenting presence and severity of PAD is measurement of ankle brachial index. A resting ABI of less than 0.9 is considered abnormal and has a sensitivity of 95% and specificity of 100% for the detection of PAD, which is much better than several standard screening tests like pap smear, fecal occult blood or Mammography. This test is useful in assessing

the prognosis in both symptomatic and asymptomatic patients and its numerical valve has a very high correlation with mortality over 5 and 10 years.

ABI's also correlate highly with the severity of PAD disease with values between 0.5 to 0.9 usually seen in patients with claudication and less than 0.5 usually seen in patients with rest pain or tissue loss28. A small group of patients with normal ABI's and intermittent claudication should have exercise ABI to increase the sensitivity for detection of PAD. This is seen in patients with high-grade aorto-iliac stenosis or occlusion associated with large arterial collaterals. These patients with normal resting ABI's and abnormal exercise ABI's also have higher mortality as compared with patients with normal exercise ABI's.

Patients with diabetes mellitus and renal failure may have falsely elevated ABI's due to non-compressible and calcified lower extremity arteries. In these patients a toe brachial index (TBI) can be measured using a small toe cuff and PPG (Photoplethesmography).

Normally systolic blood pressure in the legs and arms is similar. Indeed, ankle pressure may be slightly higher than arm pressure due to pulse-wave amplification. In the presence of haemodynamically significant stenoses, the systolic blood pressure in the leg is decreased. Thus, the ratio of ankle and brachial artery pressures is ≥ 1.0 in normal individuals and <1.0 in patients with peripheral arterial disease; a ratio of <0.5 is consistent with severe ischemia.

The exercise ABI

The exercise ABI confirms the PAD diagnosis. It is also helpful in assessing the functional severity of claudication. It can unmask PAD in cases wherein the resting ABI is normal.

Arterial Duplex Ultrasound Testing

- Duplex ultrasound of the extremities is useful to diagnose anatomic location and degree of stenosis of peripheral arterial disease.
- Duplex ultrasound is useful to provide surveillance following femoral-popliteal bypass using venous conduit (but not prosthetic grafts).
- Duplex ultrasound of the extremities can be used to select candidates for:
    (a) endovascular intervention;
    (b) surgical bypass, and
    (c) to select the sites of surgical anastomosis.

However, the data that might support use of duplex ultrasound to assess long-term patency of PTA is not robust

Magnetic Resonance Angiography (MRA)

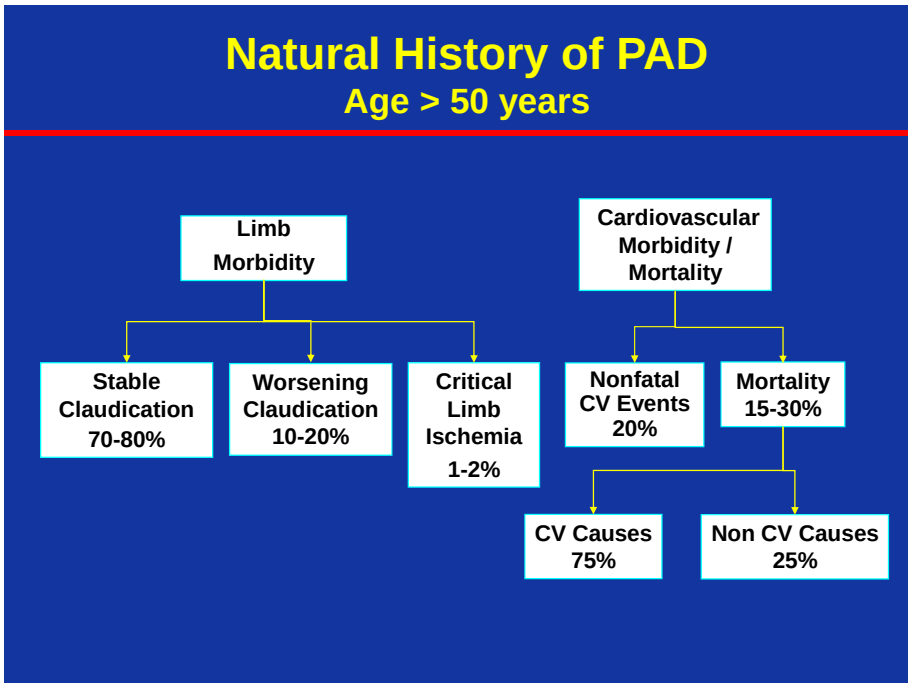
MRA of the extremities is useful to diagnose anatomic location and degree of stenosis of PAD. MRA of the extremities should be performed with a gadolinium enhancement. MRA of the extremities is useful in selecting patients with lower extremity PAD as candidates for endovascular intervention.

Computed Tomographic Angiography (CTA)

CTA of the extremities may be considered to diagnose anatomic location and presence of significant stenosis in patients with lower extremity PAD. CTA of the extremities may be considered as a substitute for MRA for those patients
with contraindications to MR

Natural History of PAD

The natural history of patients with PAD is influenced primarily by the extent of coexisting coronary artery and cerebrovascular disease. Approximately one-third to one-half of patients with symptomatic PAD have evidence of coronary artery disease based on clinical presentation and electrocardiogram, and over one- half have significant coronary artery disease by coronary angiography**.**



A Collaboration of the American College of Cardiology, the American Heart Association, the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society for Vascular Medicine and Biology, and the PAD Coalition.

Peripheral Arterial Disease Guidelines: Management of Patients with Lower Extremity PAD

Patients with PAD have a 15-30% 5 year mortality rate and two-to six fold increased risk of death from coronary heart disease. Mortality is highest in those with the most severe PAD. The likelihood of symptomatic progression of PAD appears less than the chance of succumbing to coronary artery disease. Approximately 75-80% of nondiabetic patients who present with mild to moderate claudication remain symptomatically stable. Deterioration is likely to occur in the remainder, with approximately 1-2% developing critical limb ischemia. Approximately 25% of patients with critical limb ischemia survive and undergo amputation within 1 year. The prognosis is worse in patients who continue to smoke cigarettes or who have diabetes mellitus.

Poor Prognostic features:

The following features correlate with increased incidence of future ischemic events in patients with PAD

1. ABI of less than 0.424.
2. Abnormal endothelium dependent flow mediated vasodilatation.
3. Elevated D-Dimer levels.
4. Low ADP induced platelet aggregation.

Treatment

Noncritical Ischemia

General considerations

In the general population, only approximately one-third of patients with claudication develop critical ischemia. Therefore, the treatment of noncritical

ischemia is a quality-of-life issue for most patients. Interventions such as preventive foot care, smoking cessation, and exercise can be extremely beneficial. When these interventions fail to relieve symptoms, patients are usually offered revascularization and/or medications.

Meticulous foot care is critical for the prevention of amputation. Foot care programs have been demonstrated to be extremely effective in reducing foot complications among diabetic patients without ESRD. One preventive foot care program for diabetic renal transplant recipients produced reductions in the numbers of episodes of digital gangrene and major amputations and increases in the rate of foot ulcer healing. Instruction in diabetic foot care has not figured prominently in nephrology nursing, and most dialysis units do not have a foot care program[37]. Efforts should be made to establish routine clinic-based or dialysis unit-based foot care programs for patients with ESRD and to raise physician awareness regarding the importance of preventive foot care among patients with PAOD[38].

Smoking Cessation.

One controlled non-randomized study of smoking cessation among patients with intermittent claudication reported significant improvements in walking distance among patients who stopped smoking. Smoking cessation may also slow the progression of disease and reduce the risk of amputation. The incidence of tobacco use among patients with ESRD is quite high. Of the first 1000 hemodialysis patients enrolled in the HEMO study, 52% smoked cigarettes at the time of entry into the study or had a history of tobacco use.

Despite the high prevalence of tobacco use among the ESRD population, there are no literature reports of smoking cessation programs for this group. Organized efforts to help patients with ESRD stop smoking are needed to lower overall morbidity and mortality rates, as well as those associated specifically with PAOD.

Exercise.

Exercise seems to be the most effective treatment for patients with intermittent claudication. A recent meta-analysis of 10 prospective randomized trials of exercise among patients with intermittent claudication found a weighted mean difference of 6.51 min (95% confidence interval, 4.36 to 8.66 min) in maximal walking time for the exercise group, compared with the no-treatment group[39]. Exercise produced significant improvements in maximal walking time, compared with angioplasty, at 6 months (weighted mean difference, 3.3 min; 95% confidence interval, 2.21 to 4.39 min) and did not differ significantly from surgical treatment. There have been no studies of exercise for the treatment of claudication among patients with ESRD, but there is growing evidence that exercise is beneficial in this population[40].

Medications.

Although a wide variety of medications have been used to treat PAOD, few have any proven benefit. Pentoxifylline has been widely used to treat intermittent claudication but did not produce clinically significant improvements in walking distance, compared with placebo. Pentoxifylline is renally excreted and can accumulate during moderate to severe renal insufficiency[41]. Cilostazol is a

new cAMP phosphodiesterase inhibitor that has improved absolute claudication distances in randomized, double-blind, placebo-controlled trials[42]. However, cilostazol is probably not safe for use in ESRD, because of altered protein binding. Although lipid-lowering agents are effective in the primary prevention of coronary artery disease, there is no evidence that these medications are effective in either prevention or treatment of PAOD. A recent meta-analysis of seven prospective randomized trials of lipid-lowering agents among patients with existing PAOD noted no significant improvements in pain, ABI, or skin necrosis[43]. Despite the lack of efficacy in PAOD treatment, most clinicians would prescribe lipid-lowering agents for patients with PAOD because of their proven benefits in reducing coronary artery and cerebrovascular disease in this high-risk patient group. Some data suggest that the use of aspirin alone or aspirin plus dipyridamole results in less progression of PAOD, as measured angiographically; however, there is no evidence for improved clinical outcome.

Although vitamin E, steroid sex hormones, defibrotide, garlic, and gingko biloba have been used to treat PAOD, they have no proven benefit and cannot be recommended at this time.

Ticlopidine and ginkgo biloba special extract significantly increase pain-free walking distance. Numerous other therapies, such as naftidrofuryl, pentoxifylline, garlic, testosterone, levocarnitine, propionyl-L-carnitine, and chelation therapy have been evaluated in RCTs but have not been shown to be effective or are less effective than established treatments. A variety of strategies to stimulate new collateral channels in peripheral ischemia,such as the use of growth factors and autologous bone marrow cells, are currently being evaluated.(*JAMA. 2006;295:547-553)*

Angioplasty is indicated for select patients with intermittent claudication. However, trials comparing angioplasty with exercise suggest that, although angioplasty may result in short-term improvements in walking distance, this benefit is not sustained with time[44]. Angioplasty of intermittent claudication has not been studied in patients with ESRD**.**

Surgical Revascularization.

Although critical ischemia is the only clear indication for surgical bypass, most bypass operations are performed because of intermittent claudication. For example, intermittent claudication was the indication for intervention for 73% of patients enrolled in Veterans Cooperative Study 199, a prospective randomized trial of percutaneous transluminal angioplasty (PTA) *versus* surgery to treat PAOD[45]. There are currently no data to support the use of surgical bypass, rather than exercise therapy, for the treatment of intermittent claudication in the general population. Most centres do not routinely offer revascularization procedures for patients with ESRD and claudication, but several surgical series investigating revascularization among patients with ESRD have included small numbers of patients with intermittent claudication [46]

Critical Ischemia

General Considerations.

Each year, approximately 150,000 patients develop critical limb ischemia

in the United States. The treatment of choice is a limb-salvage procedure, such as vascular reconstruction, percutaneous angioplasty, thrombolysis, or thrombectomy. However, approximately 40%; of patients are not candidates for a reopening procedure. Approximately one-half of these patients undergo primary amputation. The remaining patients either receive no treatment or, usually as a last resort, are offered nonsurgical limb-salvage therapies such as spinal cord stimulation (SCS) or intravenous prostaglandin infusion. The percentage of patients who ultimately require amputation is even higher in the ESRD population, because many of these patients are not candidates for limb-sparing procedures in the first place and many of those who do undergo revascularization subsequently require amputation.

Limb-Sparing Procedures.

Surgical Revascularization.

The current trend is to offer limb-sparing surgery to patients with critical ischemia. This approach consists of surgical bypass, which may be performed in concert with limited amputation (below the tarsal-metatarsal joint) in an attempt to avoid major amputation. The management of limb-threatening ischemia among patients with ESRD poses some unique challenges. Both dialysis and transplant patients are often at high surgical risk because of the existence of comorbid conditions. Furthermore, many surgeons have anecdotally observed that the vessels of patients with ESRD are heavily calcified, rendering lower-extremity bypass technically difficult[47]. In addition, these patients often heal poorly and have high rates of wound infections, even in the presence of a patent bypass graft.

There have been no prospective trials comparing surgical bypass with other modalities for the treatment of critical ischemia among patients with ESRD, but at least 15 retrospective surgical case series have been reported in the literature. All of those studies used graft patency, limb salvage, and patient survival rates as study end points. Six of those studies included data for non-ESRD control groups. There was considerable variation in outcomes among those studies. One year graft patency rates ranged from 53 to 90%; 1year limb salvage rates ranged from 56 to 91%; 2-yr patient survival rates ranged from 32 to 67% and 30-day operative mortality rates ranged from 0 to 13%.

. Amputation in the presence of a patent bypass graft seems to be more common among patients with ESRD[48] and among patients with chronic renal failure[49]. Graft failure is most common in the setting of frank gangrene. Differences in individual study outcomes may reflect differences in the study populations (percentages of diabetic patients, smokers, and transplant recipients), in the surgical procedures performed (percentage of revascularization procedures with distal anastomosis below the popliteal artery), and in the indications for surgery (the percentage of patients for whom the indication for surgery was gangrene).

Comparisons of outcomes weighted according to the number of patients and procedures demonstrated that patients with ESRD exhibited significantly higher 30-day operative mortality rates and lower graft patency, limb salvage, and patient survival rates, compared with control subjects without ESRD.

These observations have led to disparate recommendations in the literature. Some authors, recognizing the tremendous morbidity associated with repeated unsuccessful surgical interventions, have recommended that patients with ESRD and critical ischemia should undergo primary amputation rather than revascularization[50].

Others have suggested avoiding surgical intervention and allowing auto amputation among patients with stable gangrene who are poor surgical candidates, on the basis of data indicating poor outcomes with both surgical bypass and amputation[51]. At the opposite end of the spectrum, some authors have suggested early revascularization for patients with ESRD, on the basis of the fact that outcomes are extremely poor when ischemia is advanced.

Current practices fall somewhere in the middle of this spectrum. In the absence of frank gangrene extending above the foot, patients with ESRD and critical ischemia are generally offered revascularization when it is technically possible. Amputation is usually recommended when gangrene has extended above the middle of the foot, particularly if the patient has significant comorbidity and a sedentary lifestyle[52]. However, there is considerable clinical practice variation among individual surgeons and among centres. There is also disagreement regarding the management of failed bypass grafts among patients with ESRD.

The authors of one recent surgical series of secondary interventions for failed pedal bypass grafts recommended that patients with renal insufficiency not undergo graft revision[55]. This recommendation was based on their observation that all patients with renal insufficiency who underwent revision required major amputation within one year cost is also a consideration. If successful, revascularization is cheaper than amputation because rehabilitation costs are more modest. However, the cost and length of the hospital stay increase markedly when subsequent amputation or graft revision becomes necessary.

Unfortunately, it has proven difficult to predict which patients with ESRD will develop complications after bypass and ultimately require revision or amputation. **Korn *et al.*** observed that patients undergoing peritoneal dialysis and patients with

extensive tissue loss at the time of revascularization experienced poor outcomes after revascularization. The considerable patient morbidity and expense related to failed revascularization procedures underscore the importance of patient selection for aggressive interventions. More research is clearly needed to identify patients who are at highest risk for revascularization failure and who might be better served by primary amputation.

Angioplasty.

Percutaneous transluminal angioplasty (PTA) is used when arterial disease is localized to a vessel segment <10 cm in length. PTA of the iliac arteries produces better outcomes than does PTA of more distal arteries. Two prospective clinical trials comparing angioplasty with surgical bypass in the general population failed to demonstrate convincing differences in mortality, patency, and amputation rates between the two groups to 48 months. However, long-term follow-up monitoring in the Veterans Cooperative Study did demonstrate significantly higher 5-yr morbidity and mortality rates for the surgically treated group, compared with the angioplasty-treated group[55]. These results should be interpreted with caution; patients undergoing angioplasty may not be strictly comparable to those undergoing surgical bypass, because only a small subset of patients are candidates for angioplasty. Although some centers have experience with lower-extremity angioplasty among patients with ESRD, there have been no controlled studies of the use of angioplasty to treat PAOD among patients with ESRD, as there have been for non-ESRD patients. Furthermore, there are anecdotal reports that patients with ESRD are poor candidates for angioplasty, because of the relatively high incidence of diffuse distal lesions in this population and because of vascular calcification[55].

Spinal Cord Stimulation.

SCS has been used widely in Europe to treat persistent severe ischemic pain and ulcers in patients with critical limb ischemia not amenable to medical or surgical therapy[53]. SCS is thought to improve microcirculation by stimulating the autonomic nervous system and has been shown to increase tissue oxygenation in ischemic limbs. SCS is most effective when ulcers are small and pain control is a priority. SCS has not been systematically studied among patients with ESRD, but anecdotal reports are discouraging. For example, one study reported that all four patients with ESRD and critical ischemia who were treated with SCS eventually required amputation[55].

Prostaglandins.

Prostaglandins have been used in the treatment of both critical and noncritical ischemia, and they were demonstrated to be superior to placebo in promoting ulcer healing in several prospective, randomized, clinical trials[54]. The use of prostacyclin for dialysis patients may be problematic. Although prostacyclin has been successfully used as an extracorporeal anticoagulant for intermittent hemodialysis, careful dose adjustment is required when prostacyclin is administered in a continuous infusion because its clearance is reduced approximately fourfold in dialysis patients.

The efficacy of prostacyclin among patients with ESRD was recently called into question by a prospective, double-blind, crossover, placebo-controlled trial in five patients with ESRD and intermittent claudication. Prostacyclin had no more effect on

pain relief or walking distance than did placebo, and it was noted that prostacyclin did not produce vasodilation in these patients, as it does in non-ESRD patients[55].

Amputation.

Limb amputation is usually performed as a last resort, when conservative measures and/or revascularization have failed or when the patient is not a candidate for revascularization. Dialysis patients exhibit extremely high rates of non-traumatic lower extremity amputation resulting from all causes, compared with the general population[55]. A total of 35,898 amputations were performed in the Medicare ESRD program between 1991 and 1994. In 1994, the crude amputation rate was approximately 4.3/100 person-years for all patients with ESRD and 13.8/100 person-years for diabetic patients with ESRD. The rate of amputation in all groups increased during the period of 1991 to 1994. Amputation rates were fivefold higher for diabetic patients than for nondiabetic patients, and men were 23% more likely to undergo amputation than were women.

Poor survival rates for patients with ESRD after amputation have been well documented[55]. In the **Medicare ESRD population**, survival rates after amputation were only 32.7% at 2 years. The presence of gangrene, age of >55 yr, and below- or above-knee amputation (compared with toe amputation) were associated with significant increases in the risk of death after amputation.

Dossa *et al*[55]. noted increased hospital mortality rates and decreased long-term survival rates after amputation for patients with ESRD, compared with non-ESRD patients. For their group of 85 patients with ESRD, they recorded a hospital mortality rate of 24% and a 2-yr survival rate of 27% compared with 7 and 79% respectively for the 375 non-ESRD patients studied. Both studies noted significantly lower amputation rates for transplant recipients, compared with dialysis patients. Patients with the

highest risk of amputation after transplantation are those with coronary artery disease, those undergoing dialysis before transplantation and those with abnormal TBI and PVR values at the time of transplantation.

THERAPEUTIC ANGIOGENESIS:

This process of improving collateral vessel development holds a significant promise in patients with coronary and peripheral arterial disease. The two methods to induce angiogenesis are use of angiogenic growth factors or bone marrow mononuclear cell therapy. The benefit of using growth factor therapy with Fibroblast Growth Factor (FGF) and vascular endothelial growth factor (VEGF) - adenovirus mediated gene transfer in patients with intermittent claudication, is still controversial[56]. However in patients with CLI gene transfer using naked plasmid DNA encoding for VEGF and bone marrow mononuclear cell therapy demonstrated significant improvement in tissue loss, resolution of rest pain and lowering the level of amputation.[57]

Currently there are several controlled studies evaluating the potential role of inducing angiogenesis in these critical limb ischemia patients with hepatocyte growth factor (HGF), VEGF and FGF. The other major area is the prevention of graft disease and restenosis using antisense oligodeoxynucleotides.

MEDICAL TREATMENT OF PERIPHERAL ARTERIAL DISEASE[57]

Indication	Intervention	Method/Comment
Improving leg symptoms	Smoking cessation[36,37]	Physician advice Nicotine replacement therapy Bupropion
	Exercise[41,42]	Consider structured exercise program
	Statin drugs[44-46]	Benefit appears to be related to non–cholesterol-lowering properties of statins
	Blood pressure–lowering drugs[49-52]	Angiotensin-converting enzyme inhibitors
	Cilostazol[53]	Contraindicated in patients with heart failure
Preventing systemic complications	Smoking cessation[37]*	
	Weight loss[77,78]†	Consider in overweight patients with peripheral arterial disease
	Lowering blood pressure[66,67]	Effect determined by magnitude of blood pressure lowering
	Angiotensin-converting enzyme inhibitors[66,67]	Possible benefits beyond blood pressure–lowering effect
	Lowering blood cholesterol level[70]	
	Antiplatelet therapy[79-86]	Aspirin, with clopidogrel as suitable alternative

*No randomized evidence but based on convincing observational data.
†Efficacy unproven in randomized trials, but observational data are compelling.

4. AIM OF THE STUDY

(i) To determine the prevalence of peripheral arterial disease in chronic renal failure using the Ankle Brachial index

(ii) To correlate the prevalence of peripheral vascular disease with increasing degrees of renal insufficiency.

(iii) To study the impact of age, smoking, gender, hypertension, diabetes and ischemic heart disease on the prevalence of peripheral vascular disease in patients with chronic renal failure.

7. MATERIALS AND METHODS

Subjects: Patients attending or admitted in the department of medicine or in nephrology who fulfilled the inclusion and exclusion criteria were the subjects of the study.

Study design: cross - sectional study.

Ethical committee approval: The Ethical committee approval was obtained to carry out the study in the hospital.

Study setting: Government Rajaji Hospital Madurai.

Study duration: June 2007 – Nov 2008

Study criteria

Inclusion criteria:

1. renal insufficiency defined as an estimated Creatinine clearance of <60ml/min/1.73m^2(stages 3,4,5)

2. no previous diagnosis of Peripheral arterial disease.

Exclusion criteria:

- Patients with established diagnosis of Peripheral arterial disease
- Patients with congestive cardiac failure, aortic regurgitation, foot gangrene, connective tissue disease.
- Patients with both lower limb amputation.

Study protocol: Patients admitted/attending the outpatient department of nephrology or medicine in GRH was the study group. A well designed proforma was used to collect the demographic and clinical details of the patients.

Collaborating department:

Department of Medicine, Madurai Medical College, Madurai

Department of Nephrology, Madurai Medical College, Madurai

Department of Vascular Surgery, Madurai Medical College, Madurai.

Sample collection:

A sample of 100 patients was collected defining the stage 3-5 CKD. . Serum creatinine was measured using the modified kinetic Jaffe method. Because a number of factors, such as age, ethnicity, and gender, can influence serum creatinine, the level of kidney function was ascertained by eGFR, which was calculated using the formula that was developed and validated in the Modification of Diet in Renal Disease (MDRD) study.

The MDRD formula is as follows:

eGFR = 186.3x (serum creatinine$^{-1.154}$) x(age$^{-0.203}$) x 1.212 (if black) x0.742 (if female).

eGFR was divided into the following categories on the basis of the

National kidney Foundation guidelines:

Table 10. Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

In individuals without prevalent PAD, the ABI was determined.The ABI was obtained using the ABI TONOMETER in the Department of Vascular Surgery. The ABI attained by this method was highly accurate for it overcome the errors of manual measurement by recalibrating the ABI after E.C.G.and waveform standardization.

The systolic BP (SBP) was measured in the posterior tibial and pedal arteries of both lower limbs and the brachial artery of both upper limbs. The value of the ABI was calculated using the greater SBP obtained in the lower limbs divided by the SBP of whichever was the higher in the upper limbs. The lowest ABI so obtained for each patient was used in the subsequent statistical analyses. A value of ABI <0.9 was considered pathologically low.

Prevalent CHD was defined as a previous MI by electrocardiogram, coronary artery bypass surgery,coronary angioplasty.

Prevalent hypertension The diagnosis of hypertension required that the patient had had such a diagnosis made previously by the treating physician, a BP≥140/90 mmHg in patients without diabetes or BP≥130/80 mmHg in
patients with diabetes recorded on two separate occasions, or treatment
with antihypertensive drugs.

Prevalent diabetes was defined as a fasting serum glucose level ≥7.0 mmol/L (126 mg/dl), nonfasting glucose level ≥11.1 mmol/L (200 mg/L), participant report of a physician diagnosis of diabetes, or current use of any diabetes medication.

7.3. STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2002).**

Using this software, range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yates's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

1. OBSERVATION AND RESULTS

Table 1: Age Distribution

Age Group	Cases	
	No	**%**
Up to 30 yrs	7	7
31 – 40	23	23
41 – 50	37	37
51 – 60	16	16
Above 60	17	17
Total	100	100
Range	22-74 yrs	
Mean	47.3	
SD	11.8	

Most of the patients in the sample were in the age group of 41-50 years. The range was from 22-74 years.

Table 2: Gender

Gender	Cases	
	No	**%**
Male	92	92
Female	8	8
Total	100	100

Of the 100 patients in the sample, 92 patients were males and 8 patients were females.

Table 3: Symptoms

Symptoms	Cases	
	No	**%**
Symptomatic	7	7
Asymptomatic	93	93

Of the 100 patients with chronic kidney disease, majority (93%) did not have any symptoms pertaining to peripheral vascular disease, while 7 patients were symptomatic.

Table 4: Smoking (among Males)

Smoking among males (92)	Cases	
	No	%
Smokers	53	57.6
Non Smokers	39	42.4

All of the smokers were males.53 of the 92 male patients in the study were smokers accounting for 57.6%.

Table 5: Risk factors

Risk factor	Present		Absent	
	No	%	No	%
DM	20	20	80	80
HT	39	39	61	61
IHD	20	20	80	80

20 of the patients in the sample of 100 were diabetics, while 39 were hypertensives and 20 satisfied criteria for ischemic heart disease.

Table 6: Positive ABI

Positive ABI	Cases	
	No	**%**
Yes	29	29
No	71	71

The number of patients with a positive ABI (defined as a case of Peripheral Vascular Disease) wee 29. The prevalence of PAD in this sample of patients was 29%.

Table 7: Stage of CRF

CRF Stage	Cases	
	No	**%**
III	22	22
IV	50	50
V	28	28
Total	100	100

Of the 100 patients in this sample of CKD, 22 patients belonged to Stage III, 50 patients belonged to Stage IV and 28 patients belonged to Stage V.

Table 8: Age and PVD

Age Group	PVD			
	Present		Absent	
	No	%	No	%
Up to 30 (7)	1	14.3	6	85.7
31 – 40 (23)	6	26.1	17	73.9
41-50 (37)	12	32.4	25	67.6
51 – 60 (16)	5	31.3	11	68.8
Above 60 (17)	5	29.4	12	70.8
Mean age	48.6		46.8	
SD	10.3		12.4	
'p'	0.4288 Not Significant			

The age of patients studied ranged from 28-36 years with a mean age of 48.6 years±10.3 years. The maximum number of peripheral vascular disease occurred in the age group of 41-50 years. (n=12) There was no correlation between advancing age and ABI values.

Table 9: Gender and PVD

Sex	PVD			
	Present		Absent	
	No	%	No	%
Male (92)	26	28.3	66	71.7
Female (8)	3	37.5	5	62.5
'p'	0.6875 Not Significant			

Peripheral vascular disease was present in 28.3% of males (n=26) and 37.5% of females (n=3). Applying chi-square test, the difference did not show statistical significance (p=0.6875)

Table 10: Symptoms and PVD

Symptoms	PVD			
	Present		Absent	
	No	%	No	%
Symptomatic (7)	7	100	-	-
Asymptomatic (93)	22	23.7	71	76.3
'p'	0.0001 Significant			

Of the 100 patients screened, all the patients(n=7) who were symptomatic had peripheral vascular disease and 23.7% who were asymptomatic had peripheral vascular disease. The difference was not statistically significant as determined by the chi-square test.

The prevalence of asymptomatic peripheral vascular disease in CKD patients in the present study is 23.7%.

Table 11 : Smoking (among males) and PVD

Smoking	PVD			
	Present		Absent	
	No	%	No	%
Smokers (53)	20	37.8	33	62.2
Non Smokers (39)	6	15.4	33	84.6
'p'	0.0341 Significant			

Smokers had significantly increased risk of having low ABI compared with non-smokers.

ABI was less than 0.9 in 37.85% of smokers (n=20) whereas it was 15.4% among non-smokers (n=6). Chi-square test with Yates correction showed a $p<0.05$.

There was positive correlation between smoking and prevalence of peripheral vascular disease.

Table 12: DM and PVD

DM	PVD			
	Present		Absent	
	No	%	No	%
Present (20)	10	50	10	50
Absent (80)	19	23.8	61	76.3
'p'	0.0415 Significant			

The number of patients with diabetes having Peripheral vascular disease was 10 which accounted to 50%. Applying chi-square test the difference showed a statistical significance ($p<0.05$). Of the non-diabetic patients 23.8% developed peripheral vascular disease.

Table 13: HT and PVD

HT	PVD			
	Present		Absent	
	No	%	No	%
Present (39)	13	33.3	26	66.7
Absent (61)	16	26.2	45	73.8
'p'	0.5908 Not Significant			

39 patients had hypertension in the study group. Abnormal ABI was present in 33.3% of the hypertensive patients whereas abnormal ABI was seen in 26.2%, which had no statistical significance.

Table 14: IHD and PVD

IHD	PVD			
	Present		Absent	
	No	%	No	%
Present (20)	13	65%	7	35%
Absent (80)	26	32.5%	64	67.5%
'p'	0.0002 Significant			

20 patients in the study group had coronary artery disease. Analysis showed that of patients with ischemic heart disease 13 (65%) had peripheral vascular disease whereas 32.5% of patients without IHD had peripheral vascular disease. The difference was not found to be statistically significant.

Table 15: CRF Stage and PVD

CRF Stage	PVD				ABI	
	Present		Absent		Mean	SD
III (22)	3	13.6	19	86.4	1.02	0.14
IV (50)	16	32	34	68	0.95	0.16
V (28)	10	35.7	18	64.3	0.92	0.14
'p'	**0.0427** **Significant**					

Of the 100 patients in the study group, 50 patients had Stage 4 CKD. The prevalence of Peripheral vascular disease (ABI<0.9) was 13.6% in patients with Stage III CKD and 32and 35.7% in stage IV and stage V CKD respectively. The higher the stage of CKD, the higher the prevalence of Peripheral Vascular Disease. This correlation of PAD with increasing stages of CRF was found to be statistically significant.

9. DISCUSSION

PREVALENCE OF PAD

Of the 100 sampled patients with CKD, the prevalence of PAD in our study was 29%. This correlated with other studies as in **NHANES survey 1999-2000**[58], studies by **Guerrero et al**[59] and **De Vinuesa et al**[60], **Andrew Wilson et al**[61] in which the prevalence of PAD was 24%, 19%, 32% and 29% respectively.

AGE and PAD

The mean age group of patients in the study was 48.6 yrs and the highest number of patients was in the age group of 41-50 yrs. Of the 37 patients in this age group, 12 had peripheral vascular disease accounting for 32.4%, which was not statistically significant. Further there was no correlation between increasing age and the increased prevalence of PAD. Studies by de Vinuesa et al and Andrew Wilson et al showed that the prevalence of PAD in CKD increased with age.

The variation in this study could be explained by the smaller size of the sample as compared to the study by Wilson et al wherein the study had a sample of 1067 subjects. Further the study by Wilson et al. was in patients undergoing elective coronary angiography for exertional chest pain and/or dysnoea, a subset of patients known to have a high prevalence of PAD, significantly higher than in patients without symptoms suggestive of coronary artery disease.

The study by de Vinuesa et al had a sample size of 102, but the mean age of the sample was 70±11yrs but in our study the mean age group was 48.6 yrs which could account for the absence of correlation between increasing age and prevalence of PAD

Gender and PAD

There were 92 male and 8 female patients in the study. 26 of the 92 males and 3 out of 8 females had peripheral vascular disease which accounts for 28.3% and 37.5% respectively, none of which was statistically significant. In our study, gender was not found to be a significant risk factor for peripheral arterial disease in chronic renal failure patients.

While studies by de Vinuesa et al, Guerrero et al showed an increased prevalence of peripheral vascular disease in males, **Mostaza et al**[62] found an increased prevalence in females. The **HEMO study**[63] also does not find a significant statistical association between male sex and prevalence of PAD in patients with ESRD.

Symptomatic and Asymptomatic PAD

All symptomatic patients (7) were found to have evidence of peripheral vascular disease, while among the asymptomatic group(93), 22 had evidence of PAD accounting for about 23.7% .This is in agreement with the study by **Suominen et al**[64] in Finland wherein prevalence of PAD was significantly more among subjects with severe symptoms(rest pain, ulcers or gangrene) accounting for about 83.8%. However the number of asymptomatic patients detected to have PAD was 22 accounting for

about 23.7%. Only about 10%-30% of patients diagnosed with PAD based on ABI had classic symptoms of intermittent claudication.

SMOKING AND PAD

All the smokers in our study were males. Of the 92 male patients in the study,53 were smokers and 39 were non-smokers. 20 of the 53 smokers had peripheral vascular disease accounting for about 37.8%, which was statistically significant. The studies by RantenT et al, HEMO study and the **MERITO study**[65] are in parallel with the results of our study. The studies by Rantanen T et al showed a fivefold increase in the risk of PAD among patients with a history of smoking. The HEMO study found that smoking was associated with peripheral vascular disease among haemodialysis patients. In the MERITO study the prevalence of smoking in patients with CKD was 11.1%.

In a study by **Wilson et al.** there was no difference in pack years of smoking between subjects with GFR above or below 60ml/min/1.73m.The variation in this study could be due to the lesser number of active smokers in the group, only 10% of the 58% of smokers were active smokers, the rest 48% were ex-smokers.

DIABETES AND PAD

In our study, there were 20 diabetics of which 10 had PAD, accounting for about 50%. Among the 80 non-diabetics 19 had PAD, accounting for about 23.8%. The association with diabetes was found to be statistically significant. The percentage of diabetic patients who had peripheral vascular disease in other studies; **ARIC study**[66], MERITO study were 22% and 63.4% respectively. The HEMO study showed an independent relationship of diabetes with PAD in patients with ESRD. Studies by

Gurrero et al also revealed that a previous clinical record of diabetes increased the risk of developing PAD. **Sharad Pendsay et al**[20] found the prevalence of PAD in India to be about 3.9%. However this varies with the duration of diabetes as brought about by **Mohan et al**[16] wherein the prevalence of PAD in diabetics was 2% at diagnosis and 4% at 10years duration and 8% at 20years duration.

HYPERTENSION AND PAD

13 of the 39 patients who had hypertension had PAD which is about 33.3% which is not statistically significant. This agrees with the HEMO study wherein hypertension was not an independent risk factor for PAD in patients with ESRD.

The Data obtained in the MERITO study in a population of patients with hypertension and with no known cardiovascular disease, demonstrated that a GFR <60 ml/min per 1.73 m^2 and the presence of albuminuria, both were associated with a reduced ABI and that these relationships were independent of other classical risk factors of cardiovascular disease. More than one quarter of the participants with a reduced GFR or with albuminuria had a low ABI, and this prevalence increased up to 50% in the group of patients with both disorders. The incidence of PAD in the hypertenseive population in the ARIC study was 43%.

ISCHEMIC HEART DISEASE AND PAD

Of the 20 patients with Ischemic heart Disease 13 had PAD which amounts to about 65%, which was not statistically significant. This association of the presence of CAD and increased prevalence of PAD in our study was similar to other studies. The ARIC study, studies by Suominen et al (OR 3.44), de Vinuesa et al and Guerrero et al

wherein a strong association has been found between the presence of CAD and Peripheral vascular disease in patients with CKD.

STAGE OF CRF AND PAD

Of the 22 patients in Stage 3, 50 patients in stage 4 and 28 patients in stage 5 the prevalence of PAD in our study was 13.6%, 32% and 35.7% respectively, which shows an increased prevalence of peripheral vascular disease with increasing severity of renal failure. This was in correlation with studies by de Vinuesa et al and Guerrero et al.

LIMITATIONS

Ankle brachial index is used as the absolute criterion for diagnosing peripheral vascular disease in our study. The ankle brachial index is 95%sensitive and 99% specific for peripheral vascular disease; false positive and false negative results are possible rarely. False positive results could be ruled out by following up all abnormal ABI with Duplex ultrasonographic probe which was not done in our study. The number of false negative results could be decreased further by doing the exercise ABI, which was not done in our study.

Patients with diabetes mellitus and renal failure may have falsely elevated ABI's due to non-compressible and calcified lower extremity arteries. This would result in spuriously high ABI values ABI level (>1.5), this was not taken into consideration in our study. Further, in these patients with non-compressible vessels a

toe brachial index (TBI) can be measured using a small toe cuff and PPG (Photoplethesmography), which was not done in our study.

The patients in our study comprised mainly of those in Stage 4 or 5 and many were on intermittent dialysis. The ankle brachial index in patients on dialysis and in non-dialyzed patients varies to a considerable extent. This factor was not taken into account in our study.

CONCLUSION

i. The prevalence of peripheral vascular disease in patients with chronic renal failure was 29%

ii. There was a significant relationship between the prevalence of peripheral vascular disease and the stage of chronic renal failure, the higher the degree of renal insufficiency the higher was the prevalence of peripheral vascular disease.

iii. The prevalence of peripheral vascular disease in chronic renal failure was increased in smokers, diabetics and in patients with ischemic heart disease. Age, gender and hypertension were not associated with an increased prevalence of peripheral vascular disease in patients with chronic renal failure.

SUMMARY

The presence of peripheral vascular disease in chronic renal failure portends a dismal prognosis due to the increased morbidity and mortality from cardiovascular events. Peripheral vascular disease is asymptomatic in about 40%. . The study was designed to identify the prevalence of peripheral vascular disease in chronic renal failure, which is a a state of accelerated atherosclerosis.

A sample of 100 patients of chronic renal failure attending the outpatient department in medicine and nephrology were assessed for the prevalence of peripheral vascular disease by measuring the Ankle brachial index. Age, gender,smoking, hypertension, diabetes and ischemic heart disease profiles of the sample were analysed for association with peripheral vascular disease. Majority of the patients belonged to the age group 40-50 years. 92 were males, of these 53 were smokers. 7 patients in the sample had symptoms suggestive of peripheral vascular disease. While 20%(n=20) of patients in the sample were diabetics and 20%(n=20) had evidence of ischemic heart disease, hypertension was present in 39%(n=39) of the patients. 50% of the patients belonged to CRF stage 4. The prevalence of peripheral vascular disease as determined by and ABI<0.9 was 29%.

Data analysis was done using the Epidemeological Information Package 2002. Among the variables studied, smoking(p=0.0341), diabetes(p=0.0415), presence of IHD(p=0.008) and creatinine clearance(p=0.0002) were identified as having a significant association with increased prevalence of PAD.

All symptomatic patients had peripheral vascular disease(ABI<0.9) but of the asymptomatic patients 23.7%(n=22) had evidence of PAD. There was an inverse

correlation between creatinine clearance and the prevalence of PVD. The prevalence of PAD in South Indians is about 3.1%, while studies in the Western World do show a high degree of prevalence ranging from 20-35%.

This study did not take into account the factor of dialysis and the increased incidence of non-compressible vessels in patients with diabetes and chronic renal failure. Non-compressible vessels lead to high ABI values thereby underestimating the prevalence of PAD in this population. This study however does identify a population subset at high risk of fatal cardiovascular events even before the patient is symptomatic of lower extremity peripheral vascular disease, thus setting an opportunity for aggressive secondary modes of prevention that may delay the sequelae of catastrophic atherosclerotic events.

Further studies are essential to assess the validity of using tests such as toe brachial index and the Exercise ABI, which are not only non-invasive but also very effective in this subset (diabetics and CRF patients) where the ABI may underestimate the picture.

BIBLIOGRAPHY

1. API Textbook of Medicine, 8th edition

2. Harrison's Principles of Internal Medicine,Mark A. Creager, Joseph loscalzo; Vascular diseases of the extremities 17th edition,Part 9,Section 5,243: 1568-1570; Johanne M Bargman, Karl Skorecki, Chronic kidney disease, Part 12,274;1761-1771.

3. Suresh Chandra Dash and Sanjay K. Agarwal . Incidence of chronic kidney disease In India, Nephrology Dialysis Transplantation 2006 21(1):232-233;

4. Carter SA. J Vasc Surg 2001; 33:7

5. Centers for Disease Control and Prevention (CDC): Lower extremity

disease among persons aged 40 years with and without diabetes—United States, 1999–2002. *MMWR Morb Mortal Wkly Rep* 54: 1158–1160, 2005

6. O'Hare AM: High prevalence of peripheral arterial disease in persons with renal insufficiency: Results from the National Health and Nutrition Examination Survey *Circulation*109: 320–323, 2004.

7. Selvin E, Erlinger TP: Prevalence of and risk factors for peripheral arterial disease in the United States: Results from the National Health and Nutrition Examination Survey, 1999–2000. *Circulation* 110: 738–743, 2004

8. Mohan V, Premalatha G, Shastry NG. Peripheral vascular disease in non-insulin dependent diabetes mellitus in South India; Diabetes Research and Clinical Practice 27 (1995); 235-40.

9. Walters DP. Gatting W, Mullee MA, Hill RD. The prevalence, detection and epidemiological correlates of peripheral vascular disease: a comparison of diabetic and non diabetic subjects in an English community. Diab. Med 1992; 9: 710-5.

10. Janaka HU, Standl E, Mehnert H. peripheral vascular disease in diabetes mellitus and its relation to cardiovascular risk factors : screening with Doppler ultrasonic technique. Diabetes Care 3: 207.

11. Palumbo PJ, Melton LJ. Peripheral vascular disease and diabetes in M. I. Harris and R. F. Hamman(Eds), Diabetes in America, NIH 1985; publ no.85 –1468. National Institutes of Health, Bethesda, 15MD, 1-21.

12. USRDS 2004 Annual Data Report: Reference Tables. 2004; 335.

13. O'Hare, AM, Hsu, CY, Bacchetti, P, Johansen, KL. Peripheral vascular disease risk factors among patients undergoing hemodialysis. J Am Soc Nephrol 2002; 13:497.

14. Rajagopalan, S, Dellegrottaglie, S, Furniss, AL, et al. Peripheral arterial disease in patients with end-stage renal disease: observations from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Circulation 2006; 114:1914.

15. Lamping, DL, Constantinovici, N, Roderick, P, et al. Clinical outcomes, quality of life, and costs in the North Thames Dialysis Study of elderly people on dialysis: a prospective cohort study. Lancet 2000; 356:1543.

16. G. Premalatha, V. Mohan; Is Peripheral Vascular Disease Less Common in Indians? INT. J. DIAB. DEV. COUNTRIES (1995), VOL. 15

17. Guidelines in peripheral vascular disease – The PAD coalition

18. Strandness DE Jr., Preist RE, Gibbory GE.Combined clinical and pathologic study of diabetic and non diabetic peripheral arterial disease Diabetes 1964; 12 : 366-72.

19. Gibbons GW. The diabetic Foot, amputations and drainage of infection. J. Vasc Surg 1987; 5: 791-3.

20. Sharad Pendsay PERIPHERAL VASCULAR DISEASE (PVD) IN DIABETICS: INDIAN SCENARIO*INT. J. DIAB. DEV. COUNTRIES (1998), VOL. 18*

21. Cheung AK, Sarnak MJ, Yan G, Dwyer JT, Heyka RJ, Rocco MV, Teehan BP, Levey AS: Atherosclerotic cardiovascular disease risks in chronic hemodialysis patients. Kidney Int 58: 353–362, 2000[Medline]

22. Rostand SG, Drueke TB: Parathyroid hormone, vitamin D, and cardiovascular disease in chronic renal failure. Kidney Int 56: 383–392, 1999[Medline]

23. Savage T, Clarke AL, Giles M, Tomson CR, Raine AE: Calcified plaque is common in the carotid and femoral arteries of dialysis patients without clinical vascular disease. *Nephrol Dial Transplant* 13: 2004–2012, 1998

24. Bommer J, Strohbeck E, Goerich J, Bahner M, Zuna I: Arteriosclerosis in dialysis patients. Int J Artif Organs 19: 638–644, 1996[Medline]

25. Goodman WG, Goldin J, Kuizon BD, Yoon C, Gales B, Sider D, Wang Y, Chung J, Emerick A, Greaser L, Elashoff RM, Salusky IB: Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis;
N Engl J Med 342: 1478–1483, 2000

26. Goldsmith DJA, Covic A, Sambrook PA, Ackrill P: Vascular calcification in long-term haemodialysis patients in a single unit: A retrospective analysis.
Nephron 77: 37–43, 1997[Medline]

27. Guerin AP, London GM, Marchais SJ, Metivier F: Arterial stiffening and vascular calcifications in end-stage renal disease. *Nephrol Dial Transplant* 15: 1014–1021, 2000

28. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM: Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 99: 2434–2439, 19

29.. Lagrand WK, Visser CA, Hermens WT, Niessen HW, Verheugt FW, WolbinkGJ, Hack CE: C-reactive protein as a cardiovascular risk factor: More than an Epiphenomenon. *Circulation* 100: 96–102, 1999

30. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH: Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. *Circulation* 97: 425–428, 1998.

31. Yeun JY, Levine RA, Mantadilok V, Kaysen GA: C-reactive protein predicts all-cause and cardiovascular mortality in hemodialysis patients.
Am J Kidney Dis 35: 469–476, 2000

32. Stenvinkel P, Heimburger O, Paultre F, Diczfalusy U, Wang T, Berglund L, Jogestrand T: Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. *Kidney Int* 55: 1899–1911, 1999

33. Lye WC, Hughes K, Leong SO, Lee EJ: Lipoprotein (a) levels and clinical correlations in CAPD patients. *Adv Perit Dial* 11: 131–133, 1995

34.Lemmers MJ, Barry JM: Major role for arterial disease in morbidity and mortality after kidney transplantation in diabetic recipients. *Diabetes Care* 14: 295–301, 1991

35. Moustapha A, Gupta A, Robinson K, Arheart K, Jacobsen DW, Schreiber MJ, Dennis VW: Prevalence and determinants of hyperhomocysteinemia in hemodialysis and peritoneal dialysis. Kidney Int 55: 1470–1475, 1999[Medline]

36. Manns BJ, Burgess ED, Hyndman ME, Parsons HG, Schaefer JP, Scott-Douglas NW: Hyperhomocysteinemia and the prevalence of atherosclerotic vascular disease in patients with end-stage renal disease. Am J Kidney Dis 34: 669–677, 1999[Medline]

37. Richbourg MJ: Whatever happened to foot care? Preventing amputations in patients with end stage renal disease. EDTNA ERCA J 24: 4–10, 1998[Medline]

38. Hill MN, Feldman HI, Hilton SC, Holechek MJ, Ylitalo M, Benedict WG: Risk of foot complications in long-term diabetic patients with and without ESRD: A preliminary study. ANNA J 23: 381–386, 1996[Medline]

39. Leng GC, Fowler B, Ernst E: Exercise for intermittent claudication [Cochrane Review].In: The Cochrane Library 4, edited by Oxford, UK, Update Software, 2000

40. Painter P, Johansen K: Physical functioning in end-stage renal disease: Introduction: A call to activity. Adv Ren Replace Ther 6: 107–109, 1999[Medline]

41. Silver MR, Kroboth PD: Pentoxifylline in end-stage renal disease.

Drug Intell Clin Pharm 21: 976–978, 1987

42. Beebe HG, Dawson DL, Cutler BS, Herd JA, Strandness DEJr, Bortey EB, Forbes WP: A new pharmacological treatment for intermittent claudication: Results of a randomized, multicenter trial. *Arch Intern Med* 159: 2041–2050, 1999

43. Money SR, Herd JA, Isaacsohn JL, Davidson M, Cutler B, Heckman J, Forbes WP: Effect of cilostazol on walking distances in patients with intermittent claudication caused by peripheral vascular disease. J Vasc Surg 27: 267–274, 1998[Medline]

44. Fowkes FGR, Gillespie IN: Angioplasty (*versus* non surgical management) for intermittent claudication [Cochrane Review].In: The Cochrane Library 4,edited by Oxford, UK, Update Software, 2000

45. Wilson SE, White GH, Wolf G, Cross AP: Proximal percutaneous balloon angioplasty and distal bypass for multilevel arterial occlusion: Veterans Administration Cooperative Study No. 199. *Ann Vasc Surg* 4: 351–355, 1990

46. Harpavat M, Gahtan V, Ierardi R, Kerstein MD, Roberts AB: Does renal failure influence infrainguinal bypass graft outcome? *Am Surg* 64: 155–159, 1998

47. Ascer E, Veith FJ, Flores SA: Infrapopliteal bypasses to heavily calcified rock-like arteries: Management and results. Am J Surg 152: 220–223, 1986[Medline]

48. Reifsnyder T, Grossman JP, Leers SA: Limb loss after lower extremity bypass. Am J Surg 174: 149–151, 1997[Medline]

49. Carsten CG, Taylor SM, Langen EM, Crane MM: Factors associated with limb loss despite a patent infrainguinal bypass graft. Am Surg 64: 33–37, 1998[Medline]

50. Edwards JM, Taylor LMJr, Porter JM: Limb salvage in end-stage renal disease (ESRD): Comparison of modern results in patients with and without ESRD. *Arch Surg* 123: 1164–1168, 1988

51.Isiklar MH, Kulbaski M, MacDonald MJ, Lumsden AB: Infrainguinal bypass in end-stage renal disease: When is it justified? Semin Vasc Surg 10: 42–48, 1997[Medline]

52. J Am Soc Nephrol 12:2838-2847, 2001

53. Augustinsson LE, Linderoth B, Mannheimer C, Eliasson T: Spinal cord stimulation in cardiovascular disease. Neurosurg Clin North Am 6: 157–165, 1995[Medline]

54. Moncada S, Higgs EA: Prostaglandins in the pathogenesis and prevention of vascular disease. Blood Rev 1: 141–145, 1987[Medline]

55. Ruggenenti P, Vigano G, Mecca G, Cassina G, Remuzzi G: Failure of prostacyclin to improve peripheral arterial disease in dialysis patients.
Nephron 54: 93–94, 1990[Medline]

56. Mohler ER, 3rd, Rajagopalan S, Olin JW, Trachtenberg JD, Rasmussen H, Pak R, et al. Adenoviral-mediated gene transfer of vascular endothelial growth factor in critical limb ischemia: safety results from a phase I trial. Vasc Med 2003;8(1):9-13.

57. Graeme.J.Hankey, Paul E Norman, John W.Eikelboom et al.
JAMA. 2006; 295:547-553

58. Ann M. O'Hare, MA; David V. Glidden, Caroline S. Fox, Chi-yuan Hsu et al. High Prevalence of Peripheral Arterial Disease in Persons with Renal Insufficiency Circulation.2004; 109:320-323

59. GuerreroA, MontesR, Muñoz-Terol J, Gil-Peralta A, Toro J, Naranjo M, González-Pérez P,Martín-HerreaC, Ruiz-FernándezA. Peripheral arterial disease in patients with stages IV and V chronic renal failure. Nephrol Dial Transplant. 2006 Dec; 21(12)3525-31, Epub 2006 Aug 29

60. de Vinuesa SG, Ortega M, Martinez P, Goicoechea M, Campdera FG, Luño J. Subclinical peripheral arterial disease in patients with chronic kidney disease: prevalence and related risk factors. Circulation. 2007; 116:II_780

61. Andrew Wilson[1]; Kendall Beck[1]; Themistocles Assimes[1]; Naras Balasubramanian[1]; Jeffrey Olin[2]; John P Cooke Abstract 3451: Reduced Glomerular

Filtration Rate Independently Predicts the Diagnosis of Peripheral Arterial Disease and Extent of Coronary Artery Disease

62. Mostaza JM, Suarez C, Manzano L, Cairols M, García-Iglesias F, Sanchez-Alvarez J, Ampuero J, Godoy D, Rodriguez-Samaniego A, Sanchez-Zamorano MA; Relationship between ankle-brachial index and chronic kidney disease in hypertensive patients with no known cardiovascular disease. J Am Soc Nephrol. 2006 Dec;17(12 Suppl 3):S201-5

63. Michael V. Rocco[1], Alfred K. Cheung[2], Tom Greene[3] and Garabed Eknoyan[4]for the Hemodialysis (HEMO) Study Group[5] Nephrol Dial Transplant(2005)20:278-284

64.Suominen V, Rantanen T, Venermo M, Saarinen J, Salenius J Prevalence and Risk Factors of PAD among Patients with Elevated ABI. Eur J Vasc Endovasc Surg. 2008

65. MANZANO Luis ; MOSTAZA José Maria ; SUAREZ Carmen ; CAIROLS Marc ; REDONDO Rubén ; VALDIVIELSO Pedro ; Value of the ankle-brachial index in cardiovascular risk stratification of patients without known atherothrombotic disease

66. Beth D Weatherley, Lloyd E Chambless, Gerardo Heiss, Diane J Catellier and Curtis R Ellison; The reliability of the ankle-brachial index in the Atherosclerosis Risk in Communities (ARIC) study

BMC Cardiovascular Disorders2006, 6:7 doi: 10.1186/1471-2261-6-7

CASE PROFORMA

NAME: AGE: SEX:

OCCUPATION:

ADDRESS:

PHONE:

CONSENT:

SYMPTOMS:

SMOKING: DURATION: PACK YEARS:

ALCOHOLISM: DURATION:

DIABETES: DURATION:

SYSTEMIC HYPERTENSION:

CAD:

CVA:

PULSE:

CAROTID: FEMORAL:

BRACHIAL: POPLITEAL:

RADIAL: POSTERIOR TIBIAL

DORSALIS PEDIS:

CVS:

RS:

P/A:

CNS:

BRACHIAL BP: RIGHT LEFT

ANKLE BP: RIGHT LEFT

ABI: RIGHT LEFT

BLOOD SUGAR: FASTING POSTPRANDIAL

BLOOD UREA:

SERUM CREATININE:

ECG:

STAGE OF CRF:

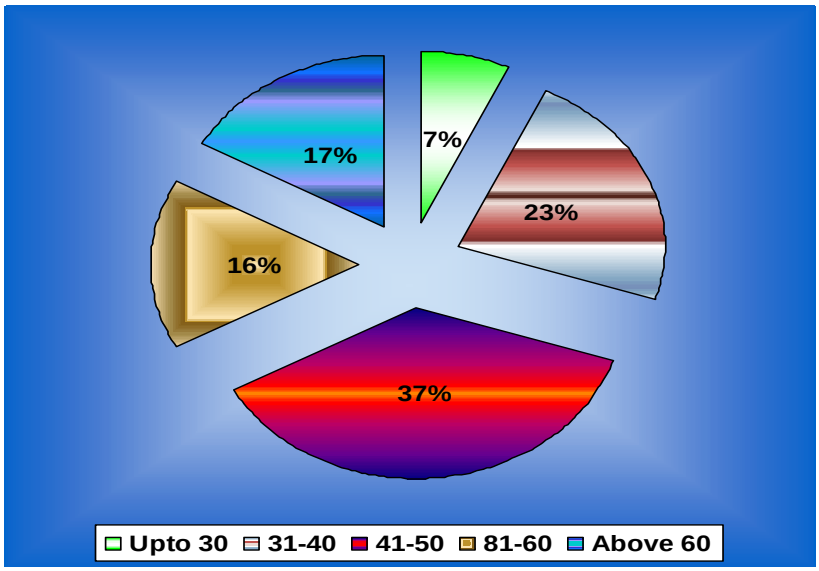
ON DIALYSIS/NOT:

ANKLE BRACHIAL INDEX:

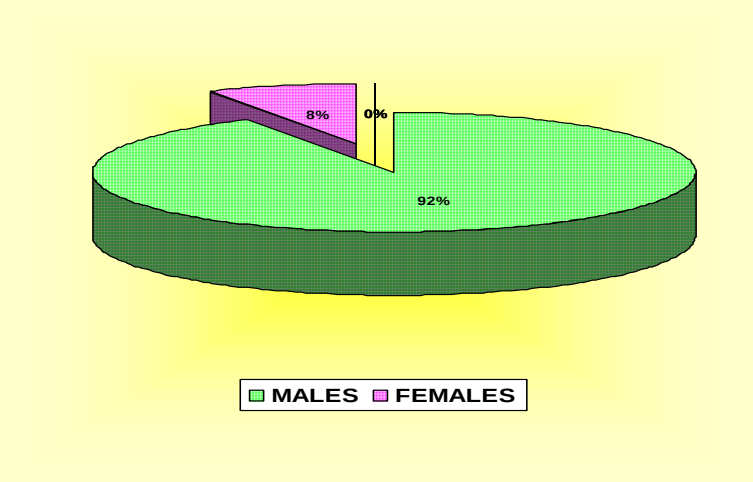
PERIPHERAL VASCULAR DISEASE:

GRAPHS

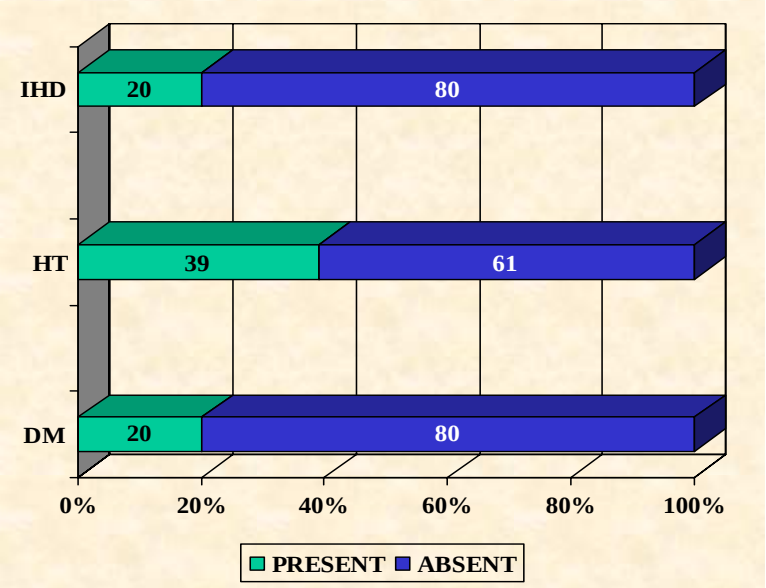
AGE DISTRIBUTION



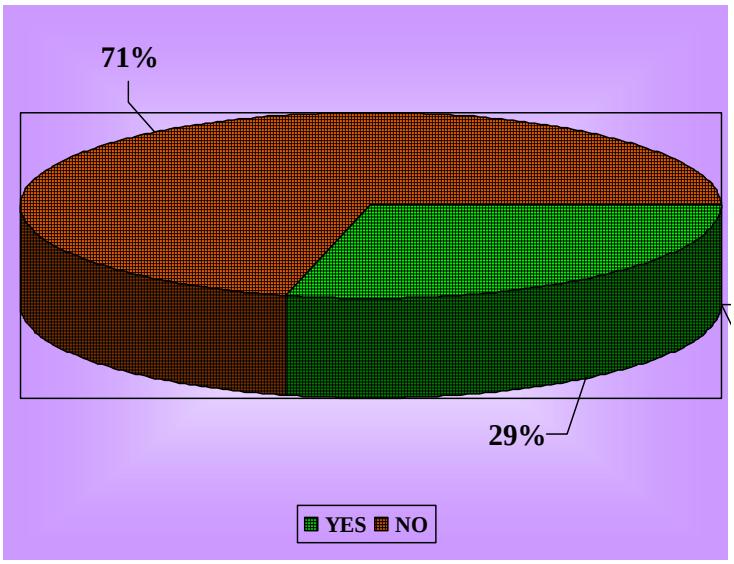
SEX DISTRIBUTION



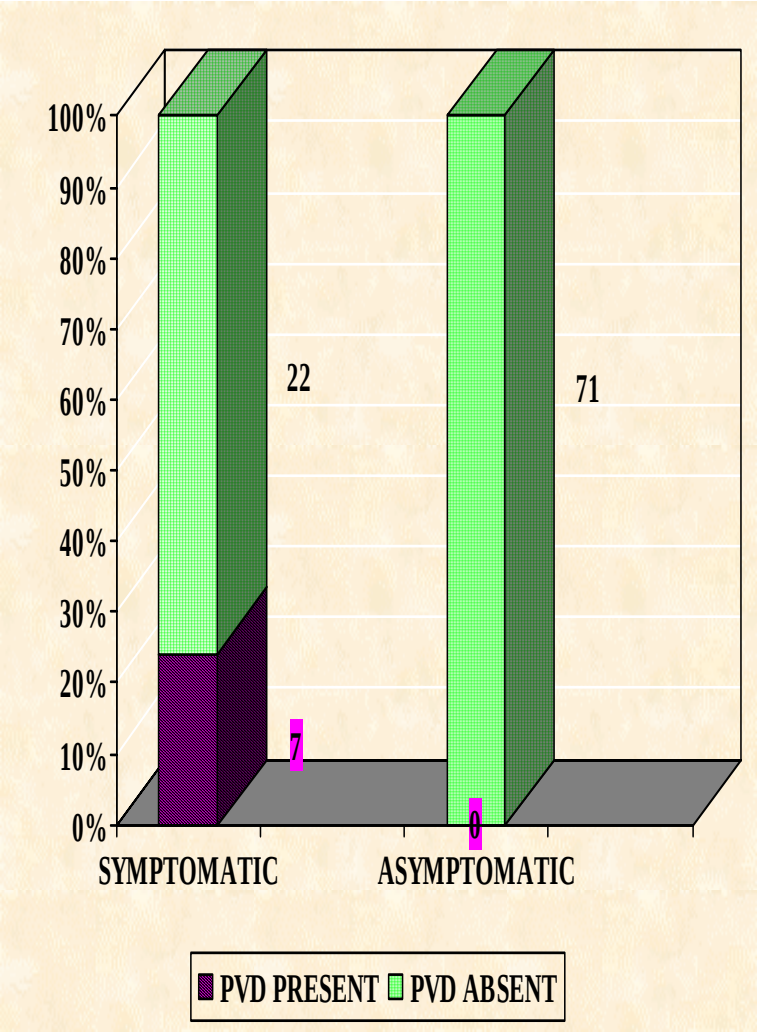
ILLNESS



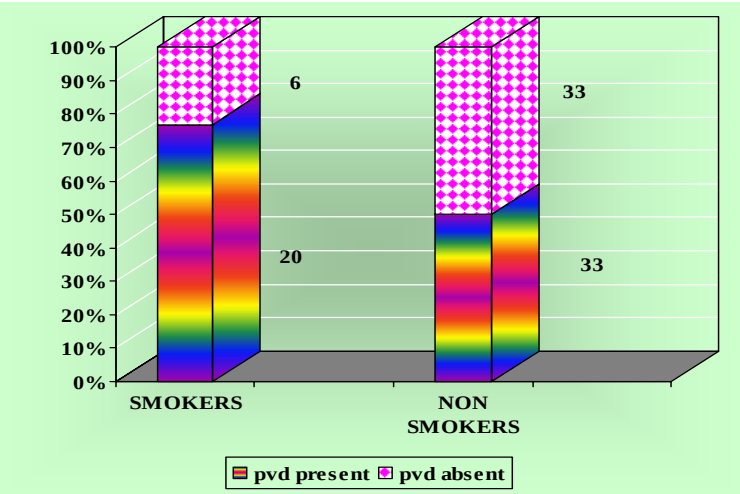
POSITIVE ABI



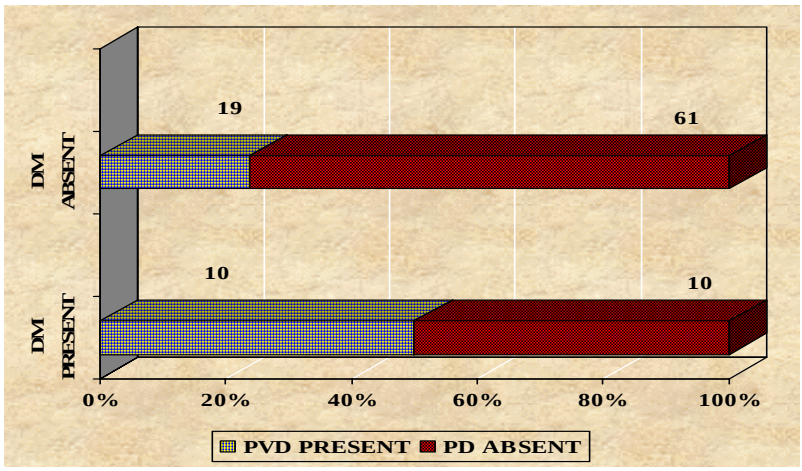
SYMPTOMS & PVD



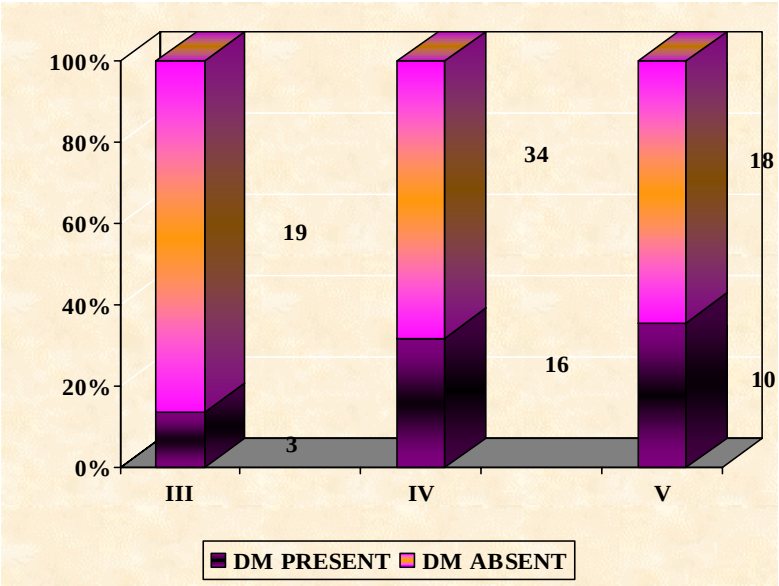
SMOKING & PVD


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
6
20
33
33
SMOKERS
NON SMOKERS
pvd present
pvd absent

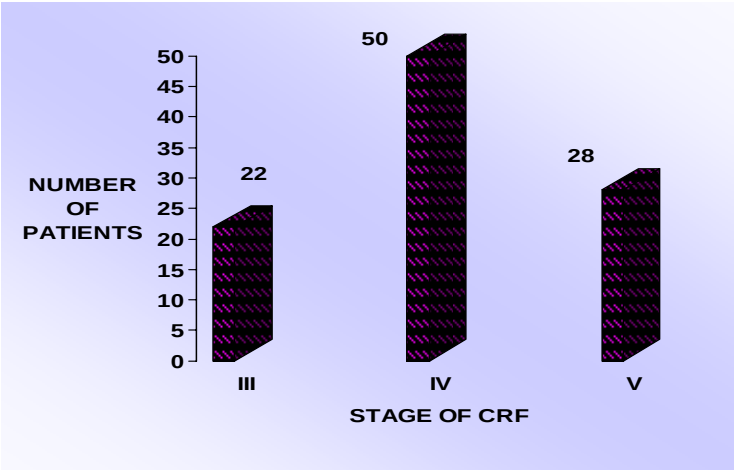
INCIDENCE OF DM & PVD



CRF STAGE & PVD



CRF STAGE


NUMBER OF PATIENTS
50
45
40
35
30
25
20
15
10
5
0
22
50
28
III
IV
V
STAGE OF CRF